IN THE CLAIMS

Amend the claims as follows.

(Currently Amended) Precursors of drugs with an anti-malarial action, characterized in that it concerns quaternary bis-ammonium salts and that they correspond to general formula (I)

in which

- \underline{A} and $\underline{A'}$ are identical to or different from one another and represent either, an $\underline{A_1}$ and $\underline{A'_1}$ group respectively, of formula

$$\int_{0}^{3}$$

where \underline{n} is an integer from 2 to 4; $\underline{R'_1}$ represents a hydrogen atom, a C1 to C5 alkyl radical, optionally substituted by an aryl radical (in particular a phenyl radical), a hydroxy, an alkoxy, in which the alkyl radical comprizes from 1 to 5 C, or aryloxy (in particular phenoxy); and \underline{W} represents a halogen atom chosen from chlorine, bromine or iodine, or a nucleofuge group, such as the tosyl $CH_3-C_6H_4-SO_3$, mesityl CH_3-SO_3 , CF_3-SO_3 , $NO_2-C_6H_4-SO_3$ radical,

or an A_2 group which represents a formyl -CHO radical,

- B and B' are identical to or different from one another and represent

either the $\underline{B_1}$ and $\underline{B'_1}$ groups respectively, if \underline{A} and $\underline{A'}$ represent $\underline{A_1}$ and $\underline{A'_1}$ respectively, $\underline{B_1}$ and $\underline{B'_1}$ representing an R_1 group which has the same definition as $\underline{R'_1}$ above, but cannot be a hydrogen atom,

or the $\underline{B_2}$ and $\underline{B'_2}$ groups respectively, if \underline{A} and $\underline{A'}$ represent $\underline{A_2}$, $\underline{B_2}$ or $\underline{B'_2}$ being the $\underline{R_1}$ group as defined above, or a group of formula

in which -Ra represents an RS- or RCO- group, where \underline{R} is a C1 to C5 alkyl radical, optionally substituted by an amino group and/or a -COOH or COOM group, where \underline{M} is a C1 to C3 alkyl; a phenyl or benzyl radical, in which the phenyl radical is optionally substituted by at least one C1 to C5 alkyl or alkoxy radical, these being optionally substituted by an amino group, or by a nitrogenous or oxygenous heterocycle, a -COOH or -COOM group; or a saturated -CH₂-heterocycle group, with 5 or 6 elements, nitrogenous and/or oxygenous; \underline{R}_2 represents a hydrogen atom, a C1 to C5 alkyl radical, or a -CH₂-COO-alkyl (C1 to C5) group; and \underline{R}_3 represents a hydrogen atom, a C1 to C5 alkyl or alkenyl radical, optionally substituted by -OH, a phosphate group, an alkoxy radical, in which the alkyl radical is C1 to C3, or an aryloxy radical; or an alkyl (or aryl), carbonyloxy group; or also \underline{R}_2 and \underline{R}_3 together form a ring with 5 or 6 carbon atoms;



- a represents

either a single bond, when \underline{A} and $\underline{A'}$ represent $\underline{A_1}$ and $\underline{A'_1}$: or when \underline{A} and $\underline{A'_1}$: or when \underline{A} and $\underline{A'_2}$ represent $\underline{A_2}$, i.e. a -CHO or -COCH₃ group, and $\underline{B_2}$ and $\underline{B'_2}$ represent

or, when \underline{A} and $\underline{A'}$ represent a –CHO group and $\underline{B_2}$ and $\underline{B'_2}$ represent $\underline{R_1}$, a group of formula

or a group of formula

in which (a) represents a bond towards \underline{Z} and (b) a bond towards the nitrogen atom.

- Z represents a C6 to C21 alkyl alkylene radical, optionally with insertion of one or more multiple bonds, and/or one or more O and/or S heteroatoms, and/or one or more aromatic rings, and the pharmaceutically acceptable salts of these compounds,

provided that R'_1 does not represent H or a C1 or C2 alkyl radical, when n=3 or 4, R_1 represents a C1 to C4 alkyl radical and Z represents a C6 to C10 alkyl radical.

2. (Original) Precursors according to claim 1, characterized in that it relates to haloalkylamines, corresponding to general formula (II)

in which \underline{R}_1 , \underline{R}'_1 , \underline{W} , \underline{n} and \underline{Z} are as defined in claim 1.

- 3. (Original) Precursors according to claim 2, characterized in that \underline{Z} represents a -(CH₂)₁₆ group.
- 4. (Original) Precursors according to claim 2 or 3, characterized in that \underline{R}_1 is a methyl radical.
- 5. (Previously Amended) Precursors according to claim 2, characterized in that \underline{R}_1 is a methyl radical and \underline{R}'_1 is either a hydrogen atom, or a methyl radical, and \underline{W} is a chlorine atom.
- 6. (Previously Amended) Precursors according to claim 2, characterized in that they are chosen from N, N'-dimethyl-N,N'-(5-chloropentyl)-1,16-

hexadecanediamine hydrochloride, or N, N'-dimethyl-N,N'-(4-chloropentyl)-1,16-hexadecanediamine hydrochloride.

7. (Original) Precursors according to claim 1, characterized in that it concerns precursors of thiazolium corresponding to general formula (III).

or to general formula (IV)

or to general formula (V)

$$R_1$$
 R_1
 R_1
 R_1
 R_2
 R_3
 R_3
 R_3
 R_3
 R_3
 R_3
 R_4
 R_4
 R_5
 R_4
 R_5
 R_6

in which \underline{R}_a , \underline{R}_1 , \underline{R}_2 , and \underline{Z} are as defined in claim 1.

- 8. (Original) Precursors according to claim 7, characterized in that they correspond to formula III in which \underline{R}_a represents an RCO- radical.
- 9. (Original) Precursors according to claim 8, characterized in that they are chosen from N,N'-diformyl-N,N'-di[1-methyl-2-S-thiobenzoyl-4-methoxybut-1-enyl]-1, 12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-S-(p-diethylaminomethylphenyl-carboxy)thio-4-methoxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-S-(p-morpholino-methylphenylcarboxy)-thio-4-methoxybut-1-enyl]-1,12-diaminododecane, and N,N'-diformyl-N,N'-di[1-methyl-2-S-thiobenzoyl-4-methoxybut-1-enyl]-1,16-diaminohexadecane.
- 10. (Original) Precursors according to claim 7, characterized in that \underline{R}_a represents \underline{RS} -.
- 11. (Original) Precursors according to claim 10, characterized in that they are chosen from N,N'-diformyl-N,N'-di[1-methyl-2-tetrahydrofurfuryl-methyldithio-4-hydroxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-propyl-dithio-4-hydroxybut-1-enyl]-1,12-diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-benzyl-dithio-4-hydroxybut-1-enyl]-1, 12 diaminododecane, N,N'-diformyl-N,N'-di[1-methyl-2-propyldithio-4-metho-xybut-1-enyl]-1, 12-diaminododecane, and N,N'-diformyl-N,N'-di[1-methyl-2-propyldithio-ethenyl]-1,12-diaminododecane.



12. (Original) Precursors according to claim 7, characterized in that they correspond to formula IV and are chosen from 2,17-(N,N'-diformyl-N,N'-dimethyl)diamino-3,16-S-thio-p-methoxybenzoyl-6,13-dioxaoctadeca-2,16-diene, 2,17-(N,N'-diformyl-N,N'-dibenzyl)diamino-3,16-S-thio-p-methoxybenzoyl-6,13-dioxaoctadeca-2,16-diene, ethyl 3,18 (N,N'-diformyl-N,N'-dimethyldiamino-4,17-S-thiobenzoyl-eicosa-3,17-dienedioate (TE12), ethyl 3,18-(N,N'-diformyl-N,N'-dibenzyl)diamino-4,17-S-thiobenzoyl-eicosa-3,17-dienedioate.

13. (Original) Precursors according to claim 7, characterized in that they correspond to formula (V) and are chosen from 2,15-(N,N'-diformyl-N,N'-dimethyl)diamino-1,16-S-thiobenzoyl-hexadeca-1,15-diene. 2,15-(N,N'-diformyl-N,N'-dibenzyl)diamino-1,16-S-thio-benzoyl-hexadeca-1,15-diene.

14. (Currently Amended) The cyclized derivatives corresponding to the precursors of thiazolium of general formula (VI)

$$R_c$$
 R_d (VI)

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in which

 \underline{R}_b represents \underline{R}_1 or \underline{T} , \underline{T} representing the group of formula

$$-Z$$
 $\stackrel{+}{\longrightarrow}$ S R_2 R_3

provided that Z does not represent a C1 to C8 <u>alkyene</u> alkyl radical, when R_c , R_d , R_1 and R_2 represent a methyl radical.

 $\underline{R_d}$ represents $\underline{R_2}$ or $\underline{P},\,\underline{P}$ representing the group of formula

 $\underline{R}_{\underline{c}}$ represents $\underline{R}_{\underline{3}}$ or U, U representing the group of formula

 \underline{R}_1 , \underline{R}_2 , \underline{R}_3 and \underline{Z} being as defined in claim 1,

 $\text{it being understood that } \underline{R}_b = \underline{T}, \text{ if } \underline{R}_c = \underline{R}_3 \text{ and } \underline{R}_d = \underline{R}_2; \ \underline{R}_d = \underline{P}, \text{ if } \underline{R}_c = \underline{R}_3 \\ \text{and } \underline{R}_b = \underline{R}_1; \text{ and } \underline{R}_c = \underline{U}, \text{ if } \underline{R}_b = \underline{R}_1, \text{ and } \underline{R}_d = \underline{R}_2.$



15. (Original) Process for obtaining precursors of thiazolium of general formula (III) to (IV) according to claim 7, characterized in that it comprises the reaction in basic medium of a thiazole derivative of formula (VI).

- 16. (Original) Process according to claim 15, characterized in that in order to obtain the compounds in which $\underline{R}_a = RCO$ -, a derivative of thiazolium of formula (VI) is reacted with an RCOR' derivative, where \underline{R} is as defined in claim 1 and \underline{R}' is a halogen atom, and in order to obtain the compounds in which $\underline{R}_a = RS$ -, said thiazolium derivatives of formula (VI) are reacted with a thiosulphate derivative RS_2O_3Na .
 - 17. (Original) Process according to claim 15 or 16, characterized in that
- in order to obtain the compounds of formula (III) a thiazole derivative suitably substituted with an alkyl dihalide is reacted, under reflux in an organic solvent, the opening of the thiazolium ring then takes place in basic medium, and by the action either of R-COCI, or of RS₂O₃N_a,

- in order to obtain the compounds of formula IV, which comprize an oxygen in the \underline{Z} chain, a thiazole derivative of general formula (VII)

1
 S 2 N₃ (VII)

3

is reacted with an alkane dihalide, in basic medium, then the addition of R_1X , the reaction medium being advantageously taken to reflux in an organic solvent, in particular alcoholic such as ethanol, for a duration sufficient to obtain the quaternization

of the nitrogen atom of the thiazole by fixing \underline{R}_1 , the opening of the thiazolium ring then being obtained in basic medium, then by the action either of R-COCI, or of RS₂O₃Na,

- in order to obtain the compounds of formula (IV) not comprizing oxygen in the \underline{Z} chain, a compound of structure

is firstly synthesized by reacting an alkyl acetoacetate with NaH, followed by alkylation, then the addition of a dihalogenoalkane, the compound obtained then being dibrominated, then thioformamide is added and, after reflux for several days, R₁X, which leads, after renewed reflux for several days, to a thiazolium, the opening of which is then carried out in basic medium, then the action of R-COCI or of R-S₂O₃N_a,

- in order to obtain the compounds of formula (V) not comprizing oxygen in the \underline{Z} chain, a $Z(CO-CH_2\ X)_2$ compound is reacted with $CH(=S)NH_2$, then R_1X is added, the opening of the thiazolium ring then being carried out in basic medium, then by adding R-COCl or $R-S_2O_3N_a$.

18. (Original) Process for obtaining haloalkylamines according to claim 1, characterized in that it comprises the alkylation of an amino alcohol of formula

by an alkyl α,ω -dihalide X-Z-X, which leads to a bis-aminoalcohol treated with a compound capable of releasing the W group.

19. (Previously Amended) Pharmaceutical compositions, characterized in that they contain an effective quantity of at least one precursor as defined in claim 1, or at least one cyclized derivative corresponding to precursors of thiazolium of general formula (VI):

$$R_c$$
 R_d (VI)

in which

 $\underline{R}_{\underline{b}}$ represents $\underline{R}_{\underline{1}}$ or \underline{T} , \underline{T} representing the group of formula:

$$-Z$$
 $\stackrel{+}{\longrightarrow}$ S _{R₂}

provided that Z does not represent a C1 to C8 alkyl radical, when R_c , R_d , R_1 and R_2 represent a methyl radical.

 $\underline{R}_{\underline{d}}$ represents $\underline{R}_{\underline{2}}$ or \underline{P} , \underline{P} representing the group of formula



 \underline{R}_c represents \underline{R}_3 or U, U representing the group of formula

 $\underline{R_1}$, $\underline{R_2}$, $\underline{R_3}$ and \underline{Z} being as defined in claim 1,

it being understood that $\underline{R}_b = \underline{T}$, if $\underline{R}_c = \underline{R}_3$ and $\underline{R}_d = \underline{R}_2$; $\underline{R}_d = \underline{P}$, if $\underline{R}_c = \underline{R}_3$ and $\underline{R}_b = \underline{R}_1$; and $\underline{R}_c = \underline{U}$, if $\underline{R}_b = \underline{R}_1$, and $\underline{R}_d = \underline{R}_2$.

in combination with a pharmaceutically inert vehicle.

20. (Currently Amended) Use for the manufacture of medicaments for the treatment of A method of treating infectious diseases dizeases, in particular maleria or babesiosis in man or animals, of comprising administering to an animal in need of said treatment a quaternary bis-ammonium salts salt of general formula I

D3

in which

- \underline{A} and $\underline{A'}$ are identical to or different from one another and represent either, an $\underline{A_1}$ and $\underline{A'_1}$ group respectively, of formula

where \underline{n} is an integer from 2 to 4; $\underline{R'_1}$ represents a hydrogen atom, a C1 to C5 alkyl radical, optionally substituted by an aryl radical (in-particular a phenyl radical), a hydroxy, an alkoxy, in which the alkyl radical comprizes from 1 to 5 C, or aryloxy (in particular phenoxy); and \underline{W} represents a halogen atom chosen from chlorine, bromine or iodine, or a nucleofuge group, such as the tosyl CH_3 - C_6H_4 - SO_3 , mesityl CH_3 - SO_3 , CF_3 - SO_3 , NO_2 - C_6H_4 - SO_3 radical.

or an \underline{A}_2 group which represents a formyl -CHO radical,

- B and B' are identical to or different from one another and represent

either the $\underline{B_1}$ and $\underline{B'_1}$ groups respectively, if \underline{A} and $\underline{A'}$ represent $\underline{A_1}$ and $\underline{A'_1}$ respectively, $\underline{B_1}$ and $\underline{B'_1}$ representing an R_1 group which has the same definition as $\underline{R'_1}$ above, but cannot be a hydrogen atom,

or the \underline{B}_2 and \underline{B}_2' groups respectively, if \underline{A} and \underline{A}' represent \underline{A}_2 , \underline{B}_2 or \underline{B}_2' being the \underline{R}_1 group as defined above, or a group of formula

in which -Ra represents an RS- or RCO- group, where \underline{R} is a C1 to C5 alkyl radical, optionally substituted by an amino group and/or a -COOH or COOM group,

where \underline{M} is a C1 to C3 alkyl; a phenyl or benzyl radical, in which the phenyl radical is optionally substituted by at least one C1 to C5 alkyl or alkoxy radical, these being optionally substituted by an amino group, or by a nitrogenous or oxygenous heterocycle, a -COOH or -COOM group; or a saturated -CH₂-heterocycle group, with 5 or 6 elements, nitrogenous and/or oxygenous; \underline{R}_2 represents a hydrogen atom, a C1 to C5 alkyl radical, or a -CH₂-COO-alkyl (C1 to C5) group; and \underline{R}_3 represents a hydrogen atom, a C1 to C5 alkyl or alkenyl radical, optionally substituted by -OH, a phosphate group, an alkoxy radical, in which the alkyl radical is C1 to C3, or an aryloxy radical; or an alkyl (or aryl), carbonyloxy group; or also \underline{R}_2 and \underline{R}_3 together form a ring with 5 or 6 carbon atoms;

- $\underline{\alpha}$ represents

either a single bond, when \underline{A} and $\underline{A'}$ represent $\underline{A_1}$ and $\underline{A'_1}$: or when \underline{A} and $\underline{A'}$ represent $\underline{A_2}$, i.e. a -CHO or -COCH₃ group, and $\underline{B_2}$ and $\underline{B'_2}$ represent

or, when \underline{A} and $\underline{A'}$ represent a -CHO group and $\underline{B_2}$ and $\underline{B'_2}$ represent $\underline{R_1}$, a group of formula

or a group of formula

in which (a) represents a bond towards \underline{Z} and (b) a bond towards the nitrogen atom.

- \underline{Z} represents a C6 to C21 <u>alkylene</u> <u>alkyl</u> radical, optionally with insertion of one or more multiple bonds, and/or one or more O and/or S heteroatoms, and/or one or more aromatic rings, and the pharmaceutically acceptable salts of these compounds, provided that R'₁ does not represent H or a C1 or C2 alkyl radical, when n = 3 or 4, R₁ represents a C1 to C4 alkyl radical and Z represents a C6 to C10 alkyl radical.

21 (Currently Amended) Pharmaceutical compositions according to claim
19, characterized in this that they can be administered by in a form which may be
administered by at least one of the oral route, by injectable route, or also by rectal route.

22. (new) A precursor according to claim 1 wherein said aryl radical is a phenyl radical.

- 23. (new) A precursor according to claim 20 wherein said aryl radical is a phenyl radical.
- 24. (new) A precursor according to claim 1 wherein said aryloxy is a phenoxy.
- 25. (new) A precursor according to claim 20 wherein said aryloxy is a phenoxy.
 - 26. (new) A method according to claim 20 wherein said animal is a man.
- 27. (new) A method according to claim 20 wherein said infections diseases are at least one of malaria and babesiosis.
- 28. (new) A method according to claim 26 wherein said infections diseases are at least one of malaria and babesiosis.

